Cardiospheres reverse adverse remodeling in chronic rat myocardial infarction: roles of soluble endoglin and Tgf-beta signaling.

Journal: Basic Res Cardiol

Publication Year: 2014

Authors: Eleni Tseliou, Heidi Reich, Geoffrey de Couto, John Terrovitis, Baiming Sun, Weixin Liu, Eduardo Marban

PubMed link: 25245471

Funding Grants: Mechanism of heart regeneration by cardiosphere-derived cells

Public Summary:
Self-assembling heart-derived stem cell clusters named cardiospheres (CSps) improve function and attenuate remodeling in rodent models of acute myocardial infarction.

Scientific Abstract:
Self-assembling heart-derived stem cell clusters named cardiospheres (CSps) improve function and attenuate remodeling in rodent models of acute myocardial infarction. The effects of CSps in chronically remodeled myocardium post-MI, and the underlying mechanisms, remain unknown. One month after permanent coronary ligation, rats were randomly assigned to injection of vehicle (controls) or CSps in the peri-infarct area. One month post-injection, CSps increased left ventricular function, reduced scar mass and collagen density, and enhanced vascularity within the infarct zone compared to controls. Immunoblots revealed Tgfbeta-1/smad cascade downregulation and an increase in soluble endoglin post-CSp injection. Six months post-transplantation, left ventricular function further improved and cardiomyocyte hypertrophy was attenuated in the CSp-treated group. In vitro, co-culture of CSps with fibroblasts recapitulated the suppression of the Tgf-beta1/smad pathway changes, responses which were blunted by neutralizing antibody against endoglin. Thus, cardiosphere transplantation enhances angiogenesis and reduces fibrosis in chronically infarcted myocardium, leading to partial reversal of cardiac dysfunction. The underlying mechanism involves inhibition of Tgf-beta1/smad signaling by CSp-secreted soluble endoglin.